REMARKS

Claims 8 and 46 have been amended to recite that the host has a condition associated with unwanted angiogenesis, support for this amendment being found in the specification in paragraph [34]. Claims15 and 47 have been amended to recite that host has a neoplastic condition, support for this amendment also being found in paragraph [34]. Claims 36 and 41 have been amended to correct typographical errors.

The amendments to the Claims detailed above are identical to those submitted in the response dated August 3, 2004 with the exception that Claim 40 now is designated appropriately as "Previously presented" as opposed to "New". As the above amendments are in compliance with 37 C.F.R. § 1.121 and introduce no new matter to the application, their entry by the Examiner is respectfully requested.

Claim Rejections - 35 USC § 102

Claims 8-11, 15-18, 35, 37, 39, 40 and 44 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Jiang et al. (Carcinogenesis 1993 14:67).

Jiang et al. is concerned with testing the ability of FK506 to prevent papilloma formation in an animal. The experimental system used by Jiang et al. is a mouse model in which repeated application of TPA to the skin of CD-1 mice (twice weekly for 22 weeks) results in papilloma formation. Jiang et al. compared papilloma formation between control mice (treated with TPA alone) or mice in which FK506 was applied to the skin 15 minutes prior to each application of TPA.

As amended, the claims of the subject application are limited to methods of inhibiting angiogenesis or tumor growth in a host having a condition associated with unwanted angiogenesis or a neoplastic condition by administering to the subject an effective amount of a Ca2+/calcineurin/NF-ATc inhibitory agent (e.g., cyclosporin). Unlike Jiang et al., the claimed invention is not drawn to preventing the formation of a papilloma/tumor (i.e., prophylactic use of FK506). Rather, the claimed invention is drawn to treating an established condition having unwanted angiogenesis or tumor growth.

In the Office Action, the Examiner asserts that Jiang et al. treat mice with existing tumors with FK506 (i.e., after week 15 some mice in the FK506 group have papillomas) and that because their data show that these mice have fewer tumors than controls, the present invention is anticipated.

However, the Applicants maintain that Jiang et al. do not show that the application of FK506 has any effect on existing papillomas. To provide such a teaching, Jiang et al. would have had to perform an experiment in which pre-existing TPA-induced papillomas were studied for their growth characteristics in the presence and absence of FK506 without further administration of TPA. The continued application of TPA throughout the papilloma formation experiment shown in Figure 1 of Jiang et al. makes it impossible to draw a conclusion as to the effect of FK506 on papilloma growth. The Applicants submit that it is entirely possible and in no way inconsistent with the asserted teachings of Jiang et al. that FK506 has no effect on the growth of TPA-induced papillomas. In light of this, the Applicants submit that the teachings of Jiang et al. simply are not drawn to the impact of FK506 on the growth of TPA-incduced papillomas.

In other words, even looking at Figure 1, one of skill in the art cannot tell whether FK506 would have any effect whatsoever on already established papillomas. This places the skilled artisan in the position of having to conceive, carry out and interpret his own experiments to determine whether FK506 can indeed inhibit the growth of existing papillomas. As such, the asserted teachings of Jiang et al. at best provide the motivation to perform such experimentation, and therefore falls far short of anticipating the claimed invention.

In fact, Jiang et al. themselves make this distinction very clear in the abstract, stating that "The effect of FK506, a potent immunosuppressive agent, on... (TPA)-promoted skin papilloma **formation** was examined in CD-1 mice" (emphasis added). Indeed, Jiang et al. are fully aware of the scope of their findings because nowhere in Jiang et al. is there any mention of the effect of FK506 on the growth of pre-existing TPA-induced papillomas. This simply was not the aim of their studies.

To reiterate, the experiments performed in Jiang et al. and the conclusions drawn therefrom are focused solely on the effect of FK506 on TPA-induced papilloma

formation and not the effect of FK506 on the growth of existing TPA-induced papillomas.

Therefore, the Applicants submit that Jiang et al. fail to teach or suggest administering an effective amount of a Ca2+/calcineurin/NF-ATc inhibitory agent to a subject having a condition of unwanted angiogenesis or a neoplastic condition for the purpose of inhibiting angiogenesis or tumor growth in the subject as is claimed in the present application. Accordingly, the Applicants respectfully request withdrawal of this rejection.

Claim Rejections - 35 USC § 103

Claims 36-44, 46 and 47 have been rejected under 35 U.S.C. § 103(a) as being obvious over Jiang et al. (Carcinogenesis 1993 14:67) in view of Flanagan et al. (Nature 1991 352:803).

As discussed above, Jiang et al. fails to teach or suggest administering an effective amount of a Ca2+/calcineurin/NF-ATc inhibitory agent to a subject having a condition of unwanted angiogenesis or a neoplastic condition for the purpose of inhibiting angiogenesis or tumor growth in the subject as is claimed in the present application. As Flanagan et al. is cited solely for its asserted teaching that FK506, cyclosporin and rapamycin have similar biologic activity, it fails to fill the fundamental deficiencies in Jiang et al. in making the claimed invention obvious.

Therefore, the Applicants submit that Claims 36-44, 46 and 47 are not obvious under 35 U.S.C. § 103(a) over Jiang et al. in view of Flanagan et al. and respectfully request withdrawal of this rejection.

CONCLUSION

In view of the amendments and remarks above, the Applicants respectfully submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 833-7770. The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN-201.

Respectfully submitted,

Date: February 23, 2005

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